REMARKS

Claim of Priority

Applicants submit herewith a copy of the cover sheet of the PCT International application from which this present application claims priority (Appendix C). The PCT International application was filed on October 18, 1999 and claimed priority to German application DE 198 47 779.1 filed on October 16, 1998. Further included is a copy of a Corrected Filing Receipt showing that the present application is a 371 of PCT/DE99/03343 and claims priority to the German application filed on October 16, 1998. As such the present application is entitled to the October 16, 1998 priority date.

Rejections of Claims and Traversal Thereof

In the October 8, 2002 Office Action,

claims 1-3 and 6-9 were rejected under 35 U.S.C. §101;

claims 1-12 were rejected under 35 U.S.C. §112, first paragraph;

claims 1, 2, 4-5 and 10 were rejected under 35 U.S.C. §102(a) as being anticipated by Muller, et al. (1998) *J. Exp. Med.* 11:2033-2045;

claims 1, 2 and 4 were rejected under 35 U.S.C. §102(b) as being anticipated by Rudert, et al. (1995) *DNA Cell. Biol.* 14, 931-937; and

claim 10 was rejected under 35 U.S.C. §102(b) as being anticipated by Fulda, et al. (1997) *Cancer Research*, 57, 3823-3829.

The rejection of claims 1-12 is hereby traversed, and reconsideration of the patentability of amended claims 1-12 is requested, in light of the ensuing remarks.

Rejection under 35 U.S.C. §101

Claims 1-12 have been amended to recite an "isolated" p53 binding region, and as such, now recite statutory subject matter. Claims 6-9 have been amended to include the process steps for the claimed process. Thus, the rejections under 35 U.S.C. §101 have been obviated and applicants request the withdrawal of same.

Rejection under 35 U.S.C. §112, first paragraph

Claims 1-12 were rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants have amended claims 1 and 2 to limit the claims to the sequences disclosed in the specification thereby obviating this rejection. Accordingly, applicants request that the rejection under 35 U.S.C. §112, first paragraph be withdrawn.

Claims 11 and 12 were rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The Office should note that applicants have amended claim 11 and canceled claim 12 but have introduced claims 23 and 24 reciting a therapeutic use of the presently claimed products. As such, the discussion set forth below relates to claims 23 and 24.

The Office has cited several references that allegedly raise questions relating to the significance of the p53-induced up-regulation of CD95 in the apoptotic response to cancer chemotherapeutic agents. Further, the Office has stated that:

> "These teachings point out the unpredictability inherent in the claimed method, as p53-induced up-regulation of CD95 has not been demonstrated to have an apoptotic effect or therapeutic potential in the absence of other cellular responses to chemotherapeutic drugs. Therefore, practicing the claimed invention as a therapeutic would require that the skilled artisan identify cells and conditions wherein the recited process would be an effective treatment. This would require significant empirical experimentation, thus placing an undue burden on one seeking to practice the invention."

Applicants assert that the present disclosure provides sufficient guidance to enable one skilled in the art to use, without undue experimentation, the p53 antigen binding regions of the present invention. For instance, applicants recognize that not all cells express p53 either due to the lack of a cell-derived p53 or that the p53 is no longer capable of inducing apoptosis. In light of this recognition, the present specification provides sufficient guidance to determine if a tumor cell expresses p53. For instance, Example 1 set forth in the specification provides a method to determine if a tumor cell produces p53 with the ability to bind to the p53 binding regions according to the present invention.

Once it is determined whether or not the tumor cell expresses p53, (Example 1A) applicants provide guidance relating to introducing an expression vector, which comprises an isolated p53 binding region of human CD95 receptor to influence apoptosis. In Example 1(B) it was shown that if the tumor cell expresses p53, the p53 binding region according to the present invention responds more intensely to apoptosis induction.

If the tumor cell does not express p53, Examples 2 and 3 provide guidance relating to introducing an expression vector comprising p53 and a p53 binding region of the presently claimed invention. Transfecting tumor cells with the expression vectors along with a reporter DNA achieved an activation of the reporter DNA that was at least twice that of the control. These results show that expression of the p53 binding receptor along with expression of p53 increased activation expression of the CD95 receptor DNA.

To demonstrate the lack of enablement, the Office must demonstrate that one of skilled in the art cannot, without undue experimentation, use the claimed isolated p53 binding regions to identify apoptosis-influencing substances. Clearly, guidance set forth in the present specification and specifically Examples 1-3 equips one skilled in the art to practice the claimed invention without undue experimentation. Further, even if some experimentation may be involved in practicing the invention, it is well settled that the enablement requirement permits some experimentation, so long as that experimentation is not undue. In *PPG Indus., Inc., v. Guardian Indus. Corp.*, 27 USPQ2d 1618, 1623 (Fed. Cir. 1996), the court stated that even where some experimentation is necessary to reduce an invention to practice, the enablement requirement is satisfied where: (1) the experimentation is routine; or (2) the specification provides "a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice

a desired embodiment of the claimed invention. Applicants satisfy these defined enablement requirements because the experimentation is routine and the examples set forth in the specification provide a reasonable amount of guidance.

Accordingly, Applicants submit that undue experimentation is not required to practice the claimed methods and respectfully request that the rejection under 35 U.S.C. §112, first paragraph be withdrawn.

Rejection under 35 U.S.C. §102(a)

Claims 1, 2, 4-5 and 10 were rejected under 35 U.S.C. §102(a) as being anticipated by Muller, et al. Applicants submit that Muller, et al was published on December 7, 1998, which was after the filing date of applicants' German priority application of October 16, 1998 as discussed above. As such, Muller, et al. is not competent prior art for a rejection under 35 U.S.C. §102(a) and applicants respectfully request that the rejection under 35 U.S.C. §102(a) be withdrawn.

Rejection under 35 U.S.C. §102(b)

Claims 1, 2 and 4 were rejected under 35 U.S.C. §102(b) as being anticipated by Rudert, et al. Applicants traverse this rejection and submit that Rudert, et al. is not anticipatory of applicants' amended claims. Examiner Sullivan found claim 3 to be novel, and as such, the sequences of claim 3 have been included in amended claim 1. Also, applicants have introduced SEQ ID. NO. 24 and 32 in claim 1 from figure 4, neither of which is disclosed in Rudert, et al. Applicants carefully reviewed the sequence of Rudert, et al. and did not locate the sequence fragment of "GGACAAGCCCTGACAAGCCA," and as such, Rudert, et al. is not anticipatory of Figure 4 and the sequences recited therein.

Claim 2, as now amended is an independent claim that is limited to the individual sequences of Figure 5, that being SEQ ID NO. 10, SEQ ID NO. 12, and SEQ ID NO. 14. Rudert, et al. does not anticipate a sequence limited to just the amino acid residues of sequences SEQ ID NO. 10, SEQ ID NO. 12, or SEQ ID NO. 14. As such, claim 2, as now amended is not anticipated by Rudert, et al. and applicants respectfully request the rejection under 35 U.S.C. §102(b) be withdrawn.

Claim 10 was rejected under 35 U.S.C. §102(b) as being anticipated by Fulda, et al. (1997). Applicants have amended claim 10, which now depends from claim 1. Claim 1 recites specific sequences that are not disclosed in Fulda, et al. and as such claim 10 as now amended is not anticipated by Fulda, et al. Applicants request that the rejection under 35 U.S.C. §102(b) be withdrawn.

Fees Payable

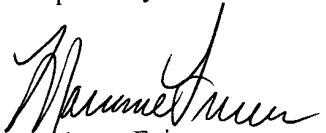
Applicants hereby petition for a one (1) month extension of time, extending the deadline for responding to the October 8, 2002 Office Action from January 8, 2003 to February 8, 2003. The entry of this petition results in a petition fee of $55.00.

Five new dependent claims have been added beyond the number for which a fee has previously been paid, resulting in an added claims fee of $45.00. A check in the amount of $100.00 is submitted herewith in payment for the additional claims and one month extension. The U.S. Patent and Trademark Office is hereby authorized to charge any additional amount necessary to the entry of this amendment, and to credit any excess payment, to Deposit Account No. 08-3284 of Intellectual Property/Technology Law.

Conclusion

Applicants have satisfied all the requirements for patentability. All pending claims are free of the art and fully comply with the requirements of 35 U.S.C. §112. It therefore is requested that Examiner Sullivan reconsider the patentability of claims 1-2, 4-11 and 13-26 in light of the distinguishing remarks herein and withdraw all rejections, thereby placing the application in condition for allowance. Notice of the same is earnestly solicited. In the event that any issues remain, Examiner Sullivan is requested to contact the undersigned attorney at (919) 419-9350 to resolve same.

Respectfully submitted,



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